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10/727,745	12/03/2003	Steffen Nock	020144-001111US	6065

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EXAMINER	
EPPERSON, JON D	

ART UNIT	PAPER NUMBER
1639	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/727,745	NOCK ET AL.	
	Examiner	Art Unit	
	Jon D. Epperson	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 January 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *20-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *03 December 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/3/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicants response filed January 10, 2008 is acknowledged

Status of the Claims

2. Claims 20-27 are pending. Applicant's election of species is acknowledged (e.g., see 1/10/08 Response, page 1). Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election of species has also been treated as an election without traverse (MPEP § 818.03(a) and/ or 37 CFR 1.111(b)). Consequently, the restriction requirement is deemed proper and made final. Claims 20-27 are examined on the merits.

Information Disclosure Statement

3. The references listed on applicant's PTO-1449 form have been considered by the Examiner. A copy of the form is attached to this Office Action (i.e., 12/3/03 IDS).

Specification

4. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claims Rejections - 35 U.S.C. 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 20-24 and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by Bonnycastle et al. (Bonnycastle et al., "Assaying Phage-Borne Peptides by Phage Capture on Fibrinogen or Streptavidin" Biol. Chem.. **1997**, 378, 509-515).

For ***claim 20***, Bonnycastle et al. (see entire document) disclose assaying phage-borne peptides by phage capture on fibrinogen or streptavidin (e.g., see Bonnycastle et al, title and abstract), which anticipates the claimed invention. For example, Bonnycastle et al. disclose **(a)** a population of replicable genetic packages each of which displays on its surface a fusion protein that comprises a surface-displayed replicable genetic package polypeptide and an exogenous polypeptide (e.g., see figure 1 showing FIBB or SAB fused to pVIII; see also page 514, column 1, Materials and Methods, Phage Clones Displaying SAB or FIBB fused to pVIII section; see also page 510, column 1, paragraph 1 wherein Applicants' elected pIII is disclosed; see also figure 2). In addition, Bonnycastle et al. disclose **(b)** a complex that comprises a target molecule and one or more members of the population of replicable genetic packages that specifically bind to said target molecule via said exogenous polypeptide (e.g., see figure 2 wherein either the Sa, Fib or Mab 17/9 represent, in the alternative, the target molecule, which is shown to be complexed to the phage particles via the SAM, FIBB or YDVPDYA, respectively). Bonnycastle et al. also disclose (c) cells in which the replicable genetic packages were amplified prior to contact with the target molecule (e.g., see page 412, column 2, first full paragraph, "A major reason for developing the phage-capture system was to bypass the

requirement for purifying phage particles [i.e., PEG purification] prior to their use in ELISAs. Figure 3A also shows that strong ELISA signals were observed from fibrinogen-captured phage bearing FIBB:pVIII phage particles, both in the presence and absence of culture medium"; see also last paragraph, "We wanted to determine whether the fibrinogen-FIBB system would capture phage directly from culture supernatants … The phage pools from the second and third rounds of panning were amplified in K91 cells bearing pBR-FIBB, then phage from the culture supernatants were directly captured on fibrinogen-coated or BSA-coated wells, and assayed by ELISA"). Thus, Bonnycastle et al. disclose the currently claimed uncleared cell culture as set forth above.

For ***claim 21***, Bonnycastle et al. also disclose the uncleared cell culture of claim 20 wherein said replicable genetic packages are selected from the group consisting of bacteriophage and eukaryotic viruses (e.g., see title and abstract; see also figure 2 wherein bacteriophage is disclosed).

For ***claim 22***, Bonnycastle et al. also disclose the uncleared cell culture of claim 20 wherein said target molecule is immobilized on a solid support (e.g., see figure 1 wherein Fib and Sa are immobilized on the bottom of the wells).

For ***claim 23***, Bonnycastle et al. also disclose the uncleared cell culture of claim 22 wherein said solid support is selected from the group consisting of a bead, a chip, a microtiter plate, a prokaryotic cell, and a eukaryotic cell (e.g., see figure 1 wherein a microtiter plate is disclosed; see also page 509; column 2, paragraph 1, "typically we perform affinity selection experiments against the peptide-library panel on microtiter plates").

For ***claim 24***, Bonnycastle et al. also disclose the uncleared cell culture of claim 20 wherein said target molecule is selected from the group consisting of a polypeptide, a nucleic acid, an RNA, a DNA, a small organic molecule and a carbohydrate (e.g., see figure 1 wherein Sib, Sa and Mab 17/9 are disclosed).

For ***claim 27***, Bonnycastle et al. also disclose the uncleared cell culture of claim 20 wherein the uncleared cell culture further comprises a detection reagent that specifically binds to the replicable genetic packages (e.g., see figure 1 wherein protein A-horse radish peroxidase (HRP) is disclosed).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 20-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over

Bonnycastle et al. (Bonnycastle et al., "Assaying Phage-Borne Peptides by Phage Capture on Fibrinogen or Streptavidin" Biol. Chem.. **1997**, 378, 509-515) in view of Cabilly I (Cabilly, S.; Heldman, J.; Katchalski-Katzir, E. "Screening Phage Display Peptide Libraries on Nitrocellulose Membranes" In: Combinatorial Peptide Library Protocols. Edited by S. Cabilly Totowa, New Jersey: Humana Press, **1998**, pages 185-194) (reference AK in the 12/3/03 IDS) and Cabilly II (Cabilly, S. "The Basic Structure of Filamentous Phage and Its Use in the Display of Combinatorial Peptide Libraries" In: Combinatorial Peptide Library Protocols. Edited by S. Cabilly Totowa, New Jersey: Humana Press, **1998**, pages 129-136) and Folgori et al. (Folgori et al., "Identification of Disease-Specific Epitopes" In: Combinatorial Peptide Library Protocols. Edited by S. Cabilly Totowa, New Jersey: Humana Press, **1998**, pages 196-208) and Tordsson et al. (Tordsson et al., "Efficient selection of scFv antibody phage by adsorption to in situ expressed antigens in tissue sections" Journal of Immunological Methods **1997**, *210*, 11-23) and Lijnen et al. (Lijnen et al., "Screening Panels of Monoclonal Antibodies Using Phage-Displayed Antigen" *Analytical Biochemistry* **1997**, *248*, 211-215).

For ***claims 20-24 and 27***, Bonnycastle et al. teach all the limitations stated in the 35 U.S.C. 102(b) rejection above (incorporated in its entirety herein by reference), which anticipates and, as a result, renders obvious claims 20-24 and 27. *Connell v. Sears, Roebuck & Co.*, 722 F.2d 1542, 1548 (Fed. Cir. 1983) ("anticipation is the epitome of obviousness"); see also *In re Skoner*, 517 F.2d 947, 950, 186 USPQ 80, 83 (CCPA 1975); *In re Pearson*, 494 F.2d 1399, 1402, 181 USPQ 641, 644 (CCPA 1974).

The prior art teaching of Bonnycastle et al. differ from the claimed invention as follows:

For ***claim 25***, Bonnycastle et al. fail to disclose the uncleared cell culture of claim 20 wherein said exogenous polypeptide is an antibody (e.g., see figure 1 wherein YDVPDY, SAV and FIBB are disclosed).

For ***claim 26***, Bonnycastle et al. fail to disclose the uncleared cell culture of claim 25 wherein said antibody is a scFv or a Fab. Bonnycastle et al. only siclsoe SAB, FIBB, YDVPDYA (e.g., see figure 1).

However, the combined references of Cabilly I, Cabilly II, Lijnen et al., Folgori et al., and Tordsson et al. teach the following limitations that are deficient in Bonnycastle et al.:

For ***claim 20***, the combined references of Cabilly I, Cabilly II, Lijnen et al., Folgori et al., and Tordsson et al. also disclose, in addition to the teachings of Bonnycastle et al. noted above, that the addition of cells in culture medium does not have a negative effect on the ELISA assay and thus need not be removed (e.g., see Cabilly I, page 191, "In our hands, the bacteria in the culture medium did not interfere with the ELISA results; however, we suggest to transfer the upper level of the culture medium to avoid most of the bacteria") (emphasis added). Thus, the combined references confirm that cell removal is not required for ELISA.

For ***claim 23***, the combined references of Cabilly I, Cabilly II, Lijnen et al., Folgori et al., and Tordsson et al. also disclose, in addition to the teachings of Bonnycastle et al. noted above, the use of other solid substrates such as Applicants' elected beads (e.g., see Folgori et al., page 196, section 2.1.3; see also page 200, section 3.1; see also page 201, section 3.1.3 and 3.1.4; see also page 206, notes 1 and 4). It is

noted that the mere substitution of one component (i.e., microtiter plate) for another (i.e., beads) to yield predictable results (i.e., support for synthesis/screening) represents a *prima facie* case of obviousness. *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385, 1395 (U.S. 2007).

For ***claims 25 and 26***, the combined references of Cabilly I, Cabilly II, Lijnen et al., Folgori et al., and Tordsson et al. disclose the uncleared cell culture of claim 20 wherein said exogenous polypeptide is an antibody (e.g., see Cabilly II, page 131, second to last paragraph, "His finding [Smith] and those that followed paved the way for the generation of phage display peptide libraries, for the display of other proteins such as various forms of Ab fragments, Ab libraries, cytokines, receptors, lectins, protease inhibitors, DNA-binding proteins, enzymes, cDNA expression libraries, and more [references numbers omitted]"; see also Tordsson et al., abstract wherein scfv is disclosed; see also Lijnen et al., abstract).

For ***claim 27***, the combined references of Cabilly I, Cabilly II, Lijnen et al., Folgori et al., and Tordsson et al. disclose, in addition to the teachings of Bonnycastle et al. noted above, the sue of Applicants' elected anti-phage M13 HRP detection reagent (e.g., see Lijnen et al., abstract; see also figure 1). It is noted that the mere substitution of one component (i.e., screening platform using protein A-HRP conjugate) for another (i.e., screening platform using anti-phage M13-HRP) to yield predictable results (i.e., detection of phage protein-ligand interactions) represents a *prima facie* case of obviousness. *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385, 1395 (U.S. 2007).

It would have been *prima facie* obvious to one of ordinary skill in the art at the

time the invention was made to express antibodies/scfv as taught by the combined references of Cabilly I, Cabilly II, Lijnen et al., Folgori et al., and Tordsson et al. on the "bifunctional" phage as taught by Bonnycastle et al. because the combined references of Cabilly I, Cabilly II, Lijnen et al., Fologori et al. and Tordsson et al. expressly state that phage can be used for this purpose (e.g., see Cabilly II, page 1321, second to last paragraph as noted above). A person of skill in the art would have been motivated to use antibodies/scfv to develop antibodies against targets (e.g., therapeutic) with high affinity and selectivity. In addition, Tordsson et al. state that scfv can be used to identify novel antigens and epitopes which are not accessible by other in vitro culture techniques including antigens whose expression is induced by epithelial cell-mesenchymal cell and cell-matrix interactions or antigens that are tightly regulated spatially or temporally during embryonic development and/or pathiophysiological processes such as tumor progression (e.g., see Tordsson et al., page 12, column 1, second to last paragraph). In addition, Bonnycastle et al. state, "our data show that the FIBB and SAB phage-capture systems are valuable as simple, efficient, and economical tools for performing phage ELISAs (e.g., see page Bonnycastle et al., page 514, column 1, paragraph 1), which would include the phage ELISAs set forth in the combined references of Cabilly I, Cabilly II, Lijnen et al., Fologori et al. and Tordsson et al. A person of ordinary skill in the art would reasonable have expected to be successful because, for example, Bonnycastle et al. state, "These phage capture systems should be compatible with a number of pVIII and pIII-based display vectors" (e.g., see Bonnycastle et al., page 514, column 1, first full paragraph), which would encompass the phage systems described by

the combined references of Cabilly I, Cabilly II, Lijnen et al., Fologori et al. and Tordsson et al. Finally, it should also be noted that the mere substitution of one component for another to yield predictable results represents a *prima facie* case of obviousness. *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385, 1395 (U.S. 2007). Here, substitution of antibodies, antibody fragments, cytokines, receptors, etc. (e.g., see Cabilly II, page 131, second to last paragraph as noted above) was well established in the art.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon D Epperson whose telephone number is (571) 272-0808. The examiner can normally be reached Monday-Friday from 9:00 to 5:30.
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz can be reached on (571) 272-0763. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Jon D. Epperson/
Primary Examiner, AU 1639